REMARKS

Claims 1-8, 15-17, and 19-28 are pending. Herein Applicant has amended the pending claims to correct certain typographical errors, to ensure consistency, and to use currently preferred terminology. None of these amendments has been made for purposes of patentability, each is fully supported by the specification and claims as originally filed, and none of them adds new matter. For the record, Applicant reserves the right to pursue in this or a related case inventive subject matter no longer or not yet claimed herein.

Applicant respectfully requests reconsideration of the invention as now claimed.

35 U.S.C. §112, First Paragraph - Enablement

Each of pending claims 1-8, 15-17, and 19-28 stands rejected because the specification allegedly fails to satisfy the "enablement" requirement of 35 U.S.C. §112, first paragraph, due to a purported failure to teach those skilled in the art how to make and use the claimed invention to prevent cardiovascular or cerebrovascular disease in a mammal, even though the Office action admits the specification is enabling with respect to treatment of such diseases. Applicant appreciates the Examiner's acknowledgement with regard to the treatment aspect of Applicant's pioneering invention, but he respectfully disagrees that the specification lacks enablement with respect to disease prevention. Contrary to statements in the Office action, the specification does, in fact, teach how to practice the claimed invention in a preventative way. For example, at page 10, lines 13-16, the specification provides, "A 'therapeutic' agent of the invention may act in a manner that is prophylactic or preventive, including those that incorporate procedures designed to target individuals that can be identified as being at risk (pharmacogenetics); ..." (emphasis added). As this passage makes clear, therapy includes (but, as indicated elsewhere in the specification, is not limited to) prevention. Shortly thereafter, the specification states, "it is believed that the level of undesirable sphingolipids such as SPH or S-1-P, and/or one or more of their metabolites, cause or contribute to the development of cardiac and myocardial diseases and disorders". Page 10, lines 23-26 (emphasis added). A short while later, the specification goes on to teach that sphingolipid-based therapies:

> "can act before such undesirable events occur or undesirable molecules are produced, and thus can prevent the occurrence of such events and/or production of such compounds to a greater degree than can be realized by therapies that act earlier in the cascade. ... Sphingolipid-based therapies provide for preventative treatments that achieve an effective state relatively quickly and non-intrusive as compared to other preventative measures, *e.g.*, changes in diet or surgery."
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> Specification page 16, line 19, through page 17, line 3 (emphasis added).

While the specification contains comparable teachings throughout, it is manifestly clear from just these representative examples that prevention is as much a part of the claimed invention as treatment, for which enablement has already been established. For this reason, Applicant respectfully submits that the specification indeed does enable the invention as claimed. He thus requests withdrawal of this rejection.

35 U.S.C. §112, First Paragraph – Written Description

Claims 1-8, 15-17, and 19-28 each purportedly fail said to satisfy the "written description" requirement of 35 U.S.C. §112, first paragraph, due to an alleged failure to use the term "small molecule" among the classes of agents useful in practicing the claimed methods. Applicant respectfully traverses, and directs the Examiner's attention, among other locations, to page 41, line 7, through page 43, line 26 (which correspond to paragraphs 122-130 in U.S. patent application publication no. 2003/0096022A1). There, the specification provides, for example:

> "The term "small molecule" includes any chemical or other moiety, other than polypeptides and nucleic acids, that can act to affect biological processes. ... Small molecules are distinguished from macromolecules by size. The small molecules of this invention usually have molecular weight less than about 5,000 daltons (Da), preferably less than about 2,500 Da, more preferably less than 1,000 Da, most preferably less than about 500 Da.
>
> "Small molecules include without limitation organic compounds peptidomimetics and conjugates thereof. As used herein, the term "organic compound" refers to any carbon-based compound other than macromolecules such nucleic acids and polypeptides."
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> '372 Application, page 41, lines 9-20 (emphasis added)

The specification then goes on to further define "organic molecule" and "peptidomimetics". *See* '372 application, page 41, line 20, through page 43, line 26.

At page 26, line 24, through page 27, line 24, of the specification, Applicant teaches,

> "One way to control the amount of undesirable sphingolipids in a patient is to alter the activity of an enzyme that catalyzes a reaction that is part of sphingolipid metabolism (see FIGS. 1 and 2). Specifically, to lower the amount of undesirable sphingolipids, one can inhibit or block enzymes involved in sphingolipid anabolism (constructive metabolism, i.e., reactions that lead to the production of undesirable sphingolipids). Additionally or alternatively, one can stimulate or activate enzymes involved in sphingolipid catabolism (destructive metabolism, i.e., reactions that lead to the breakdown of undesirable sphingolipids). For further details, see Examples 7-10."
>
> *Id.* (emphasis added)

A review of Examples 7-10 reveals extensive teachings as to ways different types of compounds, including various small molecules, can be used to modulate sphingolipid metabolism in accordance with the claimed methods.

These passages, and others in the specification, specifically alert those in the art that compounds, including small molecules, can be used in practicing Applicant's claimed invention. The specification thus demonstrates that Applicant indeed possessed this aspect of the claimed invention as of the application's filing date, thereby satisfying the "written description" requirement of 35 U.S.C. §112, first paragraph. Accordingly, this rejection should also be withdrawn.

35 U.S.C. §112, Second Paragraph

The pending claims are also said to indefinite, and thus in violation of, the requirements of 35 U.S.C. §112, second paragraph, due to the use of the terms of "small molecule" in the independent claims, "modulate" in claim 19, and the omission of ingredients other than "an agent" in claim 20. Applicant addresses each of these bases of rejection in turn, below.

With regard to "small molecule", as already noted, this term is used in many locations in the specification, and is specifically defined on page 41 of the specification as originally filed. With this and the other teachings in the specification with respect to "small molecules", Applicant respectfully submits that those ordinarily skilled in the art would understand the metes and bounds of "small molecule" in the context of Applicant's claimed invention.

Those skilled in the art would likewise understand what "modulate" means in the context of claim 19. Specifically, the term can mean either stimulation or inhibition of the activity of an

enzyme that catalyzes a reaction that produces or degrades a sphingolipid or a sphingolipid metabolite, depending on the context. For example, as taught at page 26, line 27, through page 27, line 3, of the specification, levels of undesirable sphingolipids can be lowered by inhibiting or blocking enzymes involved in sphingolipid anabolism (*i.e.*, sphingolipid production). Alternatively, one can lower sphingolipid levels by stimulating or activating enzymes involved in sphingolipid catabolism (*i.e.*, sphingolipid breakdown). *See* specification page 27, lines 3-6. Thus, while the Examiner is correct in noting that "modulate" can refer to "stimulation" or "inhibition", those in the art will certainly appreciate whether stimulation or inhibition of enzyme activity is meant in a particular context. As such, claim 19 is not indefinite.

Applicant appreciates the Examiner's comment with regard to claim 20. As the claim now makes reference to "a carrier" in addition to "an agent", Applicant respectfully submits that this basis of rejection should also be withdrawn.

For these reasons, Applicant respectfully submits that the pending claims do, in fact, the requirements of 35 U.S.C. §112, second paragraph.

35 U.S.C. §102 – Chatterjee and Miyake, et al.

Claim 20 stands separately rejected under 35 U.S.C. §102(b) as anticipated by each of two papers, the first authored by Subroto Chatterjee, the second authored by Miyake, *et al.* Applicant respectfully traverses because neither of the cited papers discloses each an every element of claim 20. Specifically, neither paper discloses a formulation that includes an agent that alters the activity or concentration of an enzyme that produces or degrades a sphingolipid or a sphingolipid metabolite to a degree necessary to achieve a therapeutic effect. As such, the neither the Chatterjee nor Miyake, *et al.* paper anticipates claim 20, meaning that each of these rejections should be withdrawn.

35 U.S.C. §103 – Non-Obviousness

Except for claim 10, all presently pending claims stand rejected under 35 U.S.C. §103(a) as being unpatentable over the Chatterjee paper in combination with the Miyake, *et al.* paper. Applicant respectfully traverses because one ordinarily skilled in the art would not be motivated to combine the Chatterjee and Miyake, *et al.* papers, and even if combined, the cited

combination does not yield a reasonable expectation of success.

With regard to the lack of motivation to combine, Applicant notes the papers relate to different enzymes, the Chatterjee paper relating to N-SMase and the Miyake, *et al.* paper to serine palmitoyl transferase. As such, no motivation exists to combine these two references. As for the required reasonable expectation of success, nothing in the Chatterjee and Miyake, *et al.* papers even suggests that Applicant's claimed invention could be successfully achieved. Because of a lack of a motivation to combine and no reasonable expectation of success, the absence of either of which alone would require a finding of non-obviousness, this rejection should also be withdrawn.

Dated: 3 May 2006

Respectfully submitted,

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